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C−H Bond Cleavage with Reductants: Re-Investigating the Reactivity of Monomeric $Mn^{III/IV}$−Oxo Complexes and the Role of Oxo Ligand Basicity

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Metal complexes with terminal oxo ligands have been implicated in a variety of oxidative transformations. For instance, monomeric oxoiron units are proposed to be the competent oxidants in many mono- and dioxygenases.[1] Similarly, numerous synthetic oxometal complexes have been shown to be involved in either C−H bond cleavage or O-atom transfer reactions.[2] Uncovering the factors that govern these processes is an active area of investigation.[3] Redox properties are normally used as a measure of function, but more recently Green has pointed out that the basicity of the terminal oxo ligand may contribute to the reactivity of oxometal complexes, especially C−H bond cleavage.[4] This premise implies that oxometal complexes could function at lower redox potentials, which is advantageous because unwanted oxidation of the surrounding moieties would be avoided, such as those within a protein active site. Goldberg[5] and Que[6] have also found that the oxo basicity can affect function in synthetic oxomanganese(V) and oxoiron(IV) complexes. In this report we describe the C−H bond cleavage for two related oxomanganese complexes with unusually low oxidation potentials but strongly basic oxo ligands. A re-evaluation of their thermodynamic properties and a new kinetic analysis point to a process whereby the basicity of the oxo ligand has a large effect on the observed oxidative chemistry.[7]

We have developed the monomeric oxomanganese complexes,[8] $[Mn^{III}H_3buea(O)]^{2-}$ and $[Mn^{IV}H_3buea(O)]^{-}$, and their related Mn−OH complexes, $[Mn^{II}H_3buea(OH)]^{2-}$ and $[Mn^{III}H_3buea(OH)]^{-}$ (Figure 1). The Mn(O(H)) complexes are distinct from other synthetic systems because of their intramolecular H-bond networks, a structural feature inspired by the active sites of metalloproteins.[9] These complexes provided us with the rare opportunity to compare the thermodynamic and kinetic properties of structurally similar oxometal complexes in different oxidation states.[10]

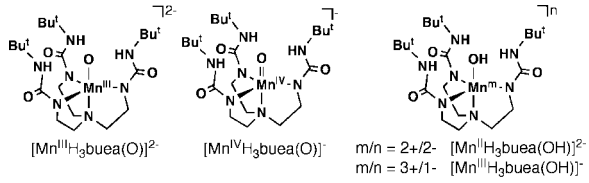
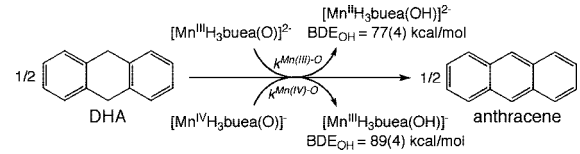


Figure 1. $Mn^{III/IV}(O)$ and $Mn^{II/III}(OH)$ complexes investigated.

Previous work has shown that the oxo ligands in the oxomanganese complexes are basic: a pK_a of 28.3 was measured in DMSO for $[Mn^{III}H_3buea(OH)]^{-}$,[11] while a p$K_a$ of ~15 was estimated for $[Mn^{IV}H_3buea(OH)]$.[12] We had incorrectly assigned the redox potentials for these complexes in early reports. A reinvestigation found that the $Mn^{III/IV}(O)$ couple is at −1.0 V and the $Mn^{IV/V}(O)$ couple is at −0.076 V.[13] Moreover, the $Mn^{II/III}(O)$ redox couple is not observed under our experimental conditions, indicating that it is < −2.0 V. Using these results, the O−H bond dissociation energy (BDE_{OH}) for $[Mn^{III}H_3buea(OH)]^{-}$ is 89 kcal/mol, lower by 21 kcal/mol relative to the value reported previously; the BDE_{OH} in $[Mn^{II}H_3buea(OH)]^{2-}$ remains at 77 kcal/mol.

Scheme 1. Reactions of DHA with the $Mn^{III/IV}(O)$ Complexes in DMSO



$[Mn^{III}H_3buea(O)]^{2-}$ and $[Mn^{IV}H_3buea(O)]^{-}$ react with a variety of different substrates with X−H bonds of <80 kcal/mol. For example, each complex oxidized 9,10-dihydroanthracene (DHA)[14] to anthracene in yields of >95% (Scheme 1).[8] The oxidation of substrates occurs even though the oxomanganese complexes have redox potentials that are normally associated with species that are reductants.[15] The low values for the relevant $E_{1/2}$ values (see above) suggested that the basicity of the oxo ligand, especially that in $[Mn^{III}H_3buea(O)]^{2-}$, may have a substantial contribution to the observed reactivity. Moreover, the basicity of the oxo ligands in $[Mn^{III}H_3buea(O)]^{2-}$ and $[Mn^{IV}H_3buea(O)]^{-}$ predict that the complexes should react differently with substrates of different acidities. In fact, reactivity differences have been observed when phenolic compounds are used as substrates. For instance, $[Mn^{III}H_3buea(O)]^{2-}$ deprotonated 2,4,6-tri-*tert*-butylphenol,[16] producing the phenolate anion and $[Mn^{III}H_3buea(OH)]^{-}$, whereas $[Mn^{IV}H_3buea(O)]^{-}$ homolytically cleaved the O−H bond, producing the phenoxyl radical and $[Mn^{III}H_3buea(OH)]^{-}$. Similar differences in reactivity were observed when indene and fluorene were used as substrates.[14,17]

To gain insight into the reactivity of the oxomanganese complexes, a kinetic analysis was conducted for the reaction involving DHA. Kinetic data were obtained by monitoring absorbance features of either $[Mn^{III}H_3buea(O)]^{2-}$ or $[Mn^{IV}H_3buea(O)]^{-}$ during their reaction with excess DHA in DMSO solutions (Figure S1). Under these conditions, all reactions exhibited pseudo-first-order kinetic data for >3 half-lives. The pseudo-first-order rate constant (k_{obs})[18] varied linearly with the concentration of DHA (Figure 2A), indicating a second-order rate law (rate = k[Mn(O) complex][DHA]). For $[Mn^{III}H_3buea(O)]^{2-}$ at 20 °C the corrected second-

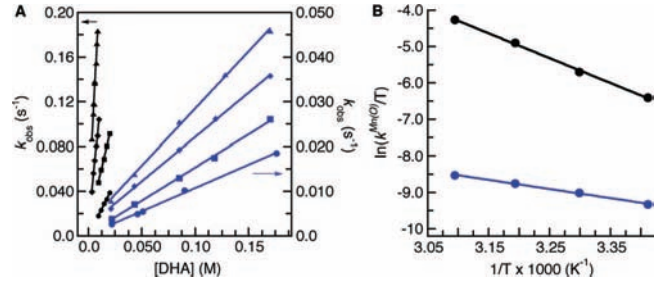


Figure 2. Kinetic data for $[Mn^{III}H_3buea(O)]^{2-}$ (black) and $[Mn^{IV}H_3buea(O)]^{-}$ (blue) at various temperatures (A) and Eyring plot (B). Temperature key (°C): 20 (●); 30 (■); 40 (◆); 50(▲).

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Table 1. Kinetic Properties of the $Mn^{III/IV}(O)$ Complexes

	$[Mn^{III}H_3buea(O)]^{2-}$	$[Mn^{IV}H_3buea(O)]^{-}$
$\Delta H^{\ddagger a}$	14(2)	5(1)
$\Delta S^{\ddagger b}$	−14(6)	−49(4)
$\Delta G^{\ddagger a,c}$	18(3)	19(2)
$k^{Mn(O)c,d}$	0.48(4)	0.026(2)
$k^{Mn(O)}{}_H/k^{Mn(O)}{}_D{}^c$	2.6	6.8

[a] kcal/mol. [b] eu. [c] 20 °C. [d] M^{-1} s^{-1}.

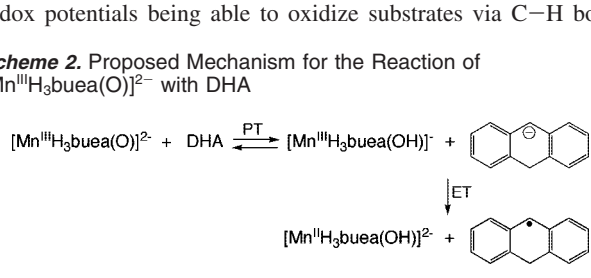
order rate constant ($k^{Mn(III)-O}$)[12,19] of 0.48(4) M^{-1} cm^{-1} is more than an *order of magnitude larger* than the $k^{Mn(IV)-O}$ of 0.026(2) M^{-1} s^{-1} found for $[Mn^{IV}H_3buea(O)]^-$ (Table 1). This result is counter to what would have been predicted based on the $BDES_{OH}$ for the Mn−OH analogues (Scheme 1), in which the BDE_{OH} of $[Mn^{III}H_3buea(OH)]^-$ is greater than that for $[Mn^{II}H_3buea(OH)]^{2-}$ by 12 kcal/mol. These data also differ from the results reported by Groves on C−H bond cleavage by oxomanganese(V/IV) porphyrin complexes, in which the Mn(V) systems react faster.[10]

The kinetic isotope effects (KIEs) for the complexes were measured at 20 °C using d_4-DHA (Table 1, Figure S3); the values obtained are indicative of primary KIEs with the value for $[Mn^{IV}H_3buea(O)]^-$ being nearly twice that of $[Mn^{III}H_3buea(O)]^{2-}$. The temperature-dependency of the rate constants was determined to probe the surprising relative rates of C−H bond cleavage by $[Mn^{III}H_3buea(O)]^{2-}$ and $[Mn^{IV}H_3buea(O)]^-$. The complexes produced linear plots of k_{obs} vs [DHA] for each temperature studied (Figure 2A, Table S1). Activation parameters were calculated from an Eyring analysis (Figure 2B, Table 1): the $\Delta H^{\ddagger}$ for the Mn(O) complexes follow the trend predicted by the BDE_{OH} values. However, there is a large difference in the entropy of activation for the two complexes [$\Delta\Delta S^{\ddagger} = -35$ eu, where $\Delta\Delta S^{\ddagger} = \Delta S^{\ddagger}(Mn^{IV}(O)) - \Delta S^{\ddagger}(Mn^{III}(O))$], which has a major effect on the relative rate constants for C−H bond cleavage.

We suggest that the observed difference in rate constants is related to the basicity of the oxo ligands, which causes the complexes to have different mechanisms. There is a large difference between the pK_a values of the C−H bonds in DHA and $[Mn^{IV}H_3buea(OH)]^-$ ($\Delta pK_a \sim 15$), resulting in $[Mn^{IV}H_3buea(O)]^-$ reacting via H-atom transfer, in which the substrate and $Mn^{IV}(O)$ complex come together in the transition state. For $[Mn^{III}H_3buea(O)]^{2-}$, the oxo ligand is significantly more basic and a two-step mechanism could occur, whereby proton transfer occurs prior to electron transfer (PT−ET, Scheme 2).[3b,7,20] The similar pK_a values for DHA and $[Mn^{III}H_3buea(OH)]^-$ ($\Delta pK_a < 2$) and the measured KIE suggest rate-limiting PT.[21] Moreover, a PT−ET path is consistent with a more positive $\Delta S^{\ddagger}$ value because an increase in charge delocalization is expected to lead to less organized solvent molecules.[22]

In summary, our results support the idea that the basicity of terminal oxo ligands in metal complexes has important effects on reactivity. This effect contributes to oxometal complexes with low redox potentials being able to oxidize substrates via C−H bond cleavage. The observation of a greater rate constant for the oxomanganese complex with the lower thermodynamic driving force for C−H bond cleavage can arise because of a mechanistic change between Mn(O) complexes. This finding offers the intriguing possibility that the basicity of the oxo ligands can significantly affect the kinetics of a reaction, a concept that may influence enzymatic activity and be used to develop new synthetic reagents.

Scheme 2. Proposed Mechanism for the Reaction of $[Mn^{III}H_3buea(O)]^{2-}$ with DHA



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Note Added after ASAP Publication. The compound name 2,4,6-tri-*tert*-phenol was incomplete in the version published ASAP February 5, 2006; the corrected name 2,4,6-tri-*tert*-butylphenol was published ASAP February 10, 2009.

Supporting Information Available: Details and figures for the kinetic experiments. This material is available free of charge via the Internet at http://pubs.acs.org.

References

(1) (a) Groves, J. T.; Han, Y. Z. In *Cytochrome P450: Structure Mechanisms and Biochemistry*; Ortiz de Montellano, P. R., Ed.; Plenum: New York, 1995; Chapter 1, pp 3−48. (b) Sono, M.; Roach, M. P.; Coulter, E. D.; Dawson, J. H. *Chem. Rev.* **1996**, *96*, 2841–2888. (c) Groves, J. T. *J. Inorg. Biochem.* **2006**, *100*, 434–447. (d) Krebs, C.; Fujimori, D. G.; Walsh, C. T.; Bollinger, J. M. *Acc. Chem. Res.* **2007**, *40*, 484–492.
(2) (a) Costas, M.; Mehn, M. P.; Jensen, M. P.; Que, L., Jr. *Chem. Rev.* **2004**, *104*, 939–986. (b) Nam, W. *Acc. Chem. Res.* **2007**, *40*, 522–531.
(3) (a) Mayer, J. M. In *Biomimetic Oxidations Catalyzed by Transition Metal Complexes*; Meunier, B., Ed.; Imperial College Press: London, 2000; pp 1−43, and references therein. (b) Mayer, J. M. *Annu. Rev. Phys. Chem.* **2004**, *55*, 363–390. (c) Fortner, K. C.; Laitar, D. S.; Muldoon, J.; Pu, L.; Braun-Sand, S. B.; Wiest, O.; Brown, S. N. *J. Am. Chem. Soc.* **2007**, *129*, 588–600.
(4) Green, M. T.; Dawson, J. H.; Gray, H. B. *Science* **2004**, *304*, 1653–1656.
(5) Lansky, D. E.; Goldberg, D. P. *Inorg. Chem.* **2006**, *45*, 5119–5125.
(6) Sastri, C. V.; Lee, J.; Oh, K.; Lee, Y. J.; Lee, J.; Jackson, T. A.; Ray, K.; Hirao, H.; Shin, W.; Halfen, J. A.; Kim, J.; Que, L., Jr.; Shaik, S.; Nam, W. *Proc. Natl. Acad. Sci. U.S.A.* **2007**, *104*, 19181–19186.
(7) For an example of this effect with a Ru−amido complex, see: Fulton, J. R.; Sklenak, S.; Bouwkamp, M. W.; Bergman, R. G. *J. Am. Chem. Soc.* **2002**, *124*, 4722–4737, and reference therein.
(8) (a) Borovik, A. S. *Acc. Chem. Res.* **2005**, *38*, 54–61, and references therein. (b) Parsell, T. H.; Behan, R. K.; Hendrich, M. P.; Green, M. T.; Borovik, A. S. *J. Am. Chem. Soc.* **2006**, *128*, 8728–8729.
(9) (a) Dawson, J. H. *Science* **1988**, *240*, 433–439. (b) Ortiz de Montellano, P. R. *Acc. Chem. Res.* **1987**, *20*, 289–294. (c) Lu, Y.; Valentine, J. S. *Curr. Opin. Struct. Biol.* **1997**, *7*, 495–500. (d) Ozaki, S.; Roach, M. P.; Matsui, T.; Watanabe, Y. *Acc. Chem. Res.* **2001**, *34*, 818–825.
(10) For an example of C−H bond cleavage with oxomanganese(IV/V) porphyrins, see: Jin, N.; Groves, J. T. *J. Am. Chem. Soc.* **1999**, *121*, 2923–2924.
(11) (a) Gupta, R.; MacBeth, C. E.; Young, V. G., Jr.; Borovik, A. S. *J. Am. Chem. Soc.* **2002**, *124*, 1136–1137. (b) Gupta, R.; Borovik, A. S. *J. Am. Chem. Soc.* **2003**, *125*, 13234–13242.
(12) See supporting information for details.
(13) Electrochemical measurements are versus Cp_2Fe^+/Cp_2Fe.
(14) Data in DMSO from Bordwell, F. G.; Cheng, J.-P.; Ji, G.-Z.; Satish, A. V.; Zhang, X. *J. Am. Chem. Soc.* **1991**, *113*, 9790–9795: DHA, $BDE_{CH} = 78$ kcal/mol, $pK_a = 30$; indene, $BDE_{CH} = 79$ kcal/mol; $pK_a = 20$; fluorene, $BDE_{CH} = 80$ kcal/mol; $pK_a = 23$.
(15) This effect has been observed in other oxometal complexes[5,6] and an iron(III) complex: Roth, J. P.; Mayer, J. M. *Inorg. Chem.* **1999**, *38*, 2760–2761.
(16) 2,4,6-Tri-*tert*-phenol: $BDE_{OH} = 85$ kcal/mol, $pK_a = 18$. Bordwell, F. G.; Zhang, X.-M. *J. Org. Chem.* **1995**, *8*, 529–535.
(17) Details of these reactions will be presented in a separate report.
(18) k_{obs} = slope/2, where the slopes are from the plots shown in Figure S2; a factor of $^1/_2$ accounts for the stoichiometry of the reaction (Scheme 1).
(19) The second-order rate constants were normalized for the four reactive C−H bonds per substrate molecule (see Table S1).
(20) Zdilla, M. J.; Dexheimer, J. L.; Abu-Omar, M. M. *J. Am. Chem. Soc.* **2007**, *129*, 11505–11511.
(21) Also consistent with this mechanism is an equilibrium being established for proton transfer, producing an equilibrium KIE.
(22) Marder, E. A.; Davidson, E. R.; Mayer, J. M. *J. Am. Chem. Soc.* **2007**, *129*, 5153–5166.

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